

REMARKS

This is a divisional application of the U.S. Application Serial No. No. 09/305,737, filed May 5, 1999, which claims the priority benefits of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999.

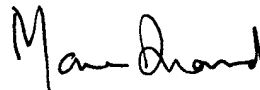
By the enclosed preliminary amendment, Claims 2-31 and 33 have been amended; and Claims 1, 32 and 36-37 have been canceled. Upon the entry of this Preliminary Amendment, Claims 2-31 and 33-35 will be pending in the present application.

Attached hereto is Appendix A captioned "Version with Markings to show changes made", and is a marked-up version of the changes made to the claims by the present amendment. In addition, for the convenience of the Examiner, all claims now pending following the entry of the present Preliminary Amendment are reproduced in Appendix B captioned "Pending Claims."

CONCLUSION

Applicants respectfully request that the application, as amended, be examined on its merits by the Examiner.

Respectfully submitted,



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APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend the text on page 1, lines 4-6 follows:

This application is a divisional application of U.S. Patent Application Serial No. 09/305,737, filed May 5, 1999 and claims the benefit under 35 U.S.C. 119(e) of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. [60/122,140] 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999, all of which are incorporated herein by reference in their entirety.

IN THE CLAIMS

Claims 1, 32 and 36-37 have been canceled

2. (Amended) The ~~compound~~ method of Claim ~~1~~ 33 wherein R³ is:
- (a) optionally substituted heterocyclyl;
 - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or SO₂NHR'R'' (where R' and R'' are independently hydrogen or alkyl);
 - (c) heteroalkyl;
 - (d) heteroalkenyl;
 - (e) heteroalkylamino;
 - (f) heteroalkoxy;
 - (g) optionally substituted heterocyclylalkyl or heterocyclyoxy;
 - (h) optionally substituted heterocyclylalkenyl;
 - (i) optionally substituted heterocyclylalkynyl;
 - (j) optionally substituted heterocyclylalkoxy;
 - (k) optionally substituted heterocyclylalkylamino;
 - (l) optionally substituted heterocyclylalkylcarbonyl;

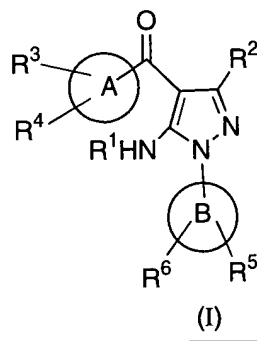
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- (k) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶ -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;
- (l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (m) arylaminoalkylene or heteroarylaminoalkylene; or
- (n) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.
3. (Amended) The ~~compound~~ method of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.
4. (Amended) The ~~compound~~ method of Claim 3 wherein A is phenyl.
5. (Amended) The ~~compound~~ method of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.
6. (Amended) The ~~compound~~ method of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.
7. (Amended) The ~~compound~~ method of Claim 5, wherein R³ is optionally substituted heteroaryl.
8. (Amended) The ~~compound~~ method of Claim 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. (Amended) The ~~compound~~ method of Claim 8, wherein R³ is at the 3-position.

10. (Amended) The ~~compound~~ method of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.
11. (Amended) The ~~compound~~ method of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.
12. (Amended) The ~~compound~~ method of Claim 5, wherein R³ is optionally substituted phenyl.
13. (Amended) The ~~compound~~ method of Claim 12, wherein R³ is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.
14. (Amended) The ~~compound~~ method of Claim 13, wherein R³ is at the 3-position.
15. (Amended) The ~~compound~~ method of Claim 14, wherein R⁵ is 4-F and R⁶ is hydrogen.
16. (Amended) The ~~compound~~ method compound of Claim 5, wherein R³ is:
- (a) heteroalkyl;
 - (b) heteroalkoxy;
 - (c) heteroalkylamino;
 - (d) optionally substituted heterocyclalkyl;
 - (e) optionally substituted heterocyclalkoxy;
 - (f) optionally substituted heterocyclalkylamino;
 - (f) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl; or
 - (h) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

17. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is heteroalkyl.
18. (Amended) The ~~compound~~ method of Claim 17, wherein R^3 is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.
19. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 2-F and R^6 is 4-F.
20. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 4-F and R^6 is hydrogen.
21. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 2-Me and R^6 is hydrogen.
22. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is heteroalkoxy or heteroalkylamino.
23. (Amended) The ~~compound~~ method of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2,2-(dihydroxymethyl)ethoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.
24. (Amended) The ~~compound~~ method of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
25. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.

26. (Amended) The ~~compound~~ method of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxy-piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.
27. (Amended) The ~~compound~~ method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
28. (Amended) The ~~compound~~ method compound of Claim 16, wherein R^3 is at the 3-position and is selected from the group consisting of (2,2-dimethyl-1,3-dioxolan-4(S)-yl)methoxy, (1,3-dioxolan-2-on-4(R)-yl)methoxy, (2-thioxo-1,3-dioxolan-4-yl)methoxy, (2,2-diethyl-1,3-dioxolan-4(S)-yl)methoxy, (2,2-diethyl-1,3-dioxolan-4(S)-yl)methylamino and (2-methyl-2-ethyl-1,3-dioxolan-4(S)-yl)methoxy.
29. (Amended) The ~~compound~~ method of Claim 28 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
30. (Amended) The ~~compound~~ method of Claim 29, wherein Y is a single bond and R^9 is SO_2R^{14} or $-SO_2NR^{15}R^{16}$.
31. (Amended) The ~~compound~~ method of Claim 30 wherein R^3 is methylsulfonylethyl or sulfamoylethyl.
33. (Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a

therapeutically effective amount of a compound of ~~Claim 1~~, selected from the group of compounds represented by Formula (I):



wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl ring;

B is an aryl;

R³ is selected from the group consisting of:

- (a) amino, alkylamino or dialkylamino;
- (b) acylamino;
- (c) optionally substituted heterocyclyl;
- (d) optionally substituted aryl or heteroaryl;
- (e) heteroalkyl;
- (f) heteroalkenyl;
- (g) heteroalkynyl;
- (h) heteroalkoxy;
- (i) heteroalkylamino;
- (j) optionally substituted heterocyclylalkyl;
- (k) optionally substituted heterocyclylalkenyl;
- (l) optionally substituted heterocyclylalkynyl;
- (m) optionally substituted heterocyclylalkoxy, cycloalkoxy or heterocyclyloxy;

- (n) optionally substituted heterocyclalkylamino;
- (o) optionally substituted heterocyclalkylcarbonyl;
- (p) heteroalkylcarbonyl;
- (q) -NHSO₂R⁶ where R⁶ is alkyl, heteroalkyl or optionally substituted heterocyclalkyl;
- (r) -NHSO₂NR⁷R⁸ where R⁷ and R⁸ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (s) -Y-(alkylene)-R⁹ where:
Y is a single bond, -O-, -NH- or -S(O)_n- (where n is an integer from 0 to 2); and
R⁹ is cyano, optionally substituted heteroaryl, -COOH, -COR¹⁰, -COOR¹¹, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹, where R¹⁰ is alkyl or optionally substituted heterocycle, R¹¹ is alkyl, and R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (t) -C(=NR²⁰)(NR²¹R²²) where R²⁰, R²¹ and R²² independently represent hydrogen, alkyl or hydroxy, or R²⁰ and R²¹ together are -(CH₂)_n- where n is 2 or 3 and R²² is hydrogen or alkyl;
- (u) -NHC(X)NR²³R²⁴ where X is -O- or -S-, and R²³ and R²⁴ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (v) -CONR²⁵R²⁶ where R²⁵ and R²⁶ independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or R²⁵ and R²⁶ together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (w) -S(O)_nR²⁷ where n is an integer from 0 to 2, and R²⁷ is alkyl, heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclalkyl, or -NR²⁸R²⁹ where R²⁸ and R²⁹ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

- (y) arylaminoalkylene or heteroarylaminoalkylene;
- (z) Z-alkylene-NR³⁰R³¹ or Z-alkylene-OR³² where Z is -NH-, -N(alkyl)- or -O-, and R³⁰, R³¹ and R³² are independently of each other, hydrogen, alkyl or heteroalkyl;
- (aa) -OC(O)-alkylene-CO₂H or -OC(O)-NR'R'' (where R' and R'' are independently hydrogen or alkyl); and
- (bb) heteroarylalkenylene or heteroarylalkynylene;

R⁴ is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R⁵ is selected from the group consisting of :

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;

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(p) heteroalkoxy; and

(q) carboxy;

R⁶ is selected from a group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

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**APPENDIX B
PENDING CLAIMS**

2. (Amended) The method of Claim 33 wherein R³ is:
- (a) optionally substituted heterocyclyl;
 - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or SO₂NHR'R'' (where R' and R'' are independently hydrogen or alkyl);
 - (c) heteroalkyl;
 - (d) heteroalkenyl;
 - (e) heteroalkylamino;
 - (f) heteroalkoxy;
 - (g) optionally substituted heterocyclylalkyl or heterocyclylloxy;
 - (h) optionally substituted heterocyclylalkenyl;
 - (i) optionally substituted heterocyclylalkynyl;
 - (j) optionally substituted heterocyclylalkoxy;
 - (k) optionally substituted heterocyclalkylamino;
 - (l) optionally substituted heterocyclylalkylcarbonyl;
 - (k) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶ -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;
 - (l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
 - (m) arylaminoalkylene or heteroarylaminomethylene; or
 - (n) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

3. (Amended) The method of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.
4. (Amended) The method of Claim 3 wherein A is phenyl.
5. (Amended) The method of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.
6. (Amended) The method of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.
7. (Amended) The method of Claim 5, wherein R³ is optionally substituted heteroaryl.
8. (Amended) The method of Claim 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. (Amended) The method of Claim 8, wherein R³ is at the 3-position.
10. (Amended) The method of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.
11. (Amended) The method of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.
12. (Amended) The method of Claim 5, wherein R³ is optionally substituted phenyl.
13. (Amended) The method of Claim 12, wherein R³ is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.
14. (Amended) The method of Claim 13, wherein R³ is at the 3-position.

15. (Amended) The method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.
16. (Amended) The method of Claim 5, wherein R^3 is:
- (a) heteroalkyl;
 - (b) heteroalkoxy;
 - (c) heteroalkylamino;
 - (d) optionally substituted heterocyclalkyl;
 - (e) optionally substituted heterocyclalkoxy; cycloalkoxy; or cycloalkylalkoxy;
 - (f) optionally substituted heterocyclalkylamino;
-Y-(alkylene)- R^9 where Y is a single bond, -O- or -NH- and
 R^9 is optionally substituted heteroaryl, $-\text{CONR}^{12}\text{R}^{13}$, SO_2R^{14} , $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$,
 $\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19}
are independently of each other hydrogen, alkyl or heteroalkyl; or
 - (h) Z-alkylene- $\text{NR}^{30}\text{R}^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are
independently of each other, hydrogen, alkyl or heteroalkyl.
17. (Amended) The method of Claim 16, wherein R^3 is heteroalkyl.
18. (Amended) The method of Claim 17, wherein R^3 is at the 3-position and is
selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-
dimethylaminobutyl, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-
hydroxybutyl.
19. (Amended) The method of Claim 18, wherein R^5 is 2-F and R^6 is 4-F.
20. (Amended) The method of Claim 18, wherein R^5 is 4-F and R^6 is hydrogen.
21. (Amended) The method of Claim 18, wherein R^5 is 2-Me and R^6 is hydrogen.

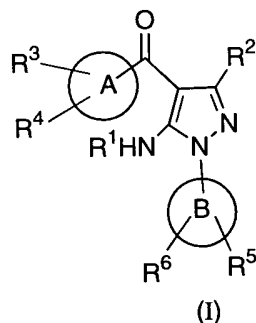
22. (Amended) The method of Claim 16, wherein R^3 is heteroalkoxy or heteroalkylamino.
23. (Amended) The method of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2,2-(dihydroxymethyl)ethoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.
24. (Amended) The method of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
25. (Amended) The method of Claim 16, wherein R^3 is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.
26. (Amended) The method of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.
27. (Amended) The method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
28. (Amended) The method of Claim 16 wherein R^3 is -Y-(alkylene)- R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, $-\text{CONR}^{12}\text{R}^{13}$, SO_2R^{14} , $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$, $-\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

29. (Amended) The method of Claim 28, wherein Y is a single bond and R⁹ is -SO₂R¹⁴ or -SO₂NR¹⁵R¹⁶.

30. (Amended) The method of Claim 29 wherein R³ is methylsulfonylethyl or sulfamoylethyl.

31. (Amended) The method of Claim 32 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

33. (Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R³ is selected from the group consisting of:

- (a) amino, alkylamino or dialkylamino;
- (b) acylamino;

- (c) optionally substituted heterocyclyl;
(d) optionally substituted aryl or heteroaryl;
(e) heteroalkyl;
(f) heteroalkenyl;
(g) heteroalkynyl;
(h) heteroalkoxy;
(i) heteroalkylamino;
(j) optionally substituted heterocyclylalkyl;
(k) optionally substituted heterocyclylalkenyl;
(l) optionally substituted heterocyclylalkynyl;
(m) optionally substituted heterocyclylalkoxy, cycloalkoxy, or heterocycliloxy;
(n) optionally substituted heterocyclylalkylamino;
(o) optionally substituted heterocyclylalkylcarbonyl;
(p) heteroalkylcarbonyl;
(q) $\text{-NHSO}_2\text{R}^6$ where R^6 is alkyl, heteroalkyl or optionally substituted heterocyclylalkyl;
(r) $\text{-NHSO}_2\text{NR}^7\text{R}^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;
(s) -Y-(alkylene)-R^9 where:
Y is a single bond, -O- , -NH- or $\text{-S(O)}_n\text{-}$ (where n is an integer from 0 to 2); and
 R^9 is cyano, optionally substituted heteroaryl, -COOH , -COR^{10} , -COOR^{11} , $\text{-CONR}^{12}\text{R}^{13}$, $\text{-SO}_2\text{R}^{14}$, $\text{-SO}_2\text{NR}^{15}\text{R}^{16}$, $\text{-NHSO}_2\text{R}^{17}$ or $\text{-NHSO}_2\text{NR}^{18}\text{R}^{19}$, where R^{10} is alkyl or optionally substituted heterocycle, R^{11} is alkyl, and R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;
(t) $\text{-C(=NR}^{20})(\text{NR}^{21}\text{R}^{22})$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $\text{-(CH}_2)_n\text{-}$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;

- (u) $\text{-NHC(X)NR}^{23}\text{R}^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (v) $\text{-CONR}^{25}\text{R}^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (w) $\text{-S(O)}_n\text{R}^{27}$ where n is an integer from 0 to 2, and R^{27} is alkyl, heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclalkyl, or $\text{-NR}^{28}\text{R}^{29}$ where R^{28} and R^{29} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (y) arylaminoalkylene or heteroarylaminomalkylene;
- (z) Z-alkylene- $\text{NR}^{30}\text{R}^{31}$ or Z-alkylene- OR^{32} where Z is -NH-, -N(alkyl)- or -O-, and R^{30} , R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;
- (aa) $\text{-OC(O)-alkylene-CO}_2\text{H}$ or -OC(O)-NR'R'' (where R' and R'' are independently hydrogen or alkyl); and
- (bb) heteroarylalkenylene or heteroarylalkynylene;
- R^4 is selected from the group consisting of:
- (a) hydrogen;
 - (b) halo;
 - (c) alkyl;
 - (d) alkoxy; and
 - (e) hydroxy;

R^5 is selected from the group consisting of :

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;

- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34. (As filed) The method of Claim 33 wherein the disease is an inflammatory disease.

35. (As filed) The method of Claim 34 wherein the disease is arthritis.

* * * * *